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10/604,779	08/15/2003	Matt Ewert	USF-196TCXC1	1778

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EXAMINER	
HOBBS, LISA JOE	

ART UNIT	PAPER NUMBER
1657	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/604,779	EWERT ET AL.	
	Examiner	Art Unit	
	Lisa J. Hobbs	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-6,8,10,12-14,16-20,23-26,33-46,48-50,64 and 65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-6,8,10,12-14,16-20,23-26,33-46,48-50,64 and 65* is/are rejected.

7)☒ Claim(s) *1,4-6,8,10,12-14,16-20,23-26,33-46,48-50 and 64* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Claims 1, 4-6, 8-10, 12-14, 16-20, 23-26, 33-46, 48-50, 64-65 are active in the case. Claims 23, 7, 11, 15, 21-22, 27-32, 47, 51-63 have been cancelled by preliminary amendment. Claims 1, 4-6, 8-10, 12-14, 16-20, 23-26, 33-46, 48-50, 64-65 are under examination; no claims are withdrawn as drawn to a non-elected invention.

Objections and Rejections Withdrawn

Any objection or rejection that has not been restated from a previous action in the instant action has been withdrawn in light of additional information, applicant's arguments or amendments to the claims and specification.

Objections to Claims

Claims 1, 4-6, 8-10, 12-14, 16-20, 23-26, 33-46, 48-50, 64-65 are objected to because of the following informalities:

Claims 1, 4-6, 8-10, 12-14, 16-20, 23-26, 33-46, 48-50, 64-65 have inconsistencies in naming of chemical compounds or enzymes. For example, some of the claims use capital letters to designate the names of chemical compounds and enzyme and other claims use small letters to designate the same compounds, and some claims recite chemicals and solutions using written names (sodium chloride, potassium phosphate) and other claims recite the same chemicals and solutions using chemical notation (NaCl, Na_3PO_4). As well, with the varied capitalization, it is unclear if the reference is to a specific enzyme or to a general type of enzyme, for example,

claim 17 refers to using 200-4,999 U of Endonuclease while claim 10 refers to exposing the whole blood sample to "an endonuclease". There is not consistency or uniformity of naming, which makes mapping the claims, searching for prior art, and checking for proper dependencies difficult. Appropriate correction is required.

Claim 50 is objected to because the amendment removing of "a DNase" leaves the word "and". The word "and" should also be deleted.

Objections to Specification

The specification is objected to because of the following informalities:

(a) The specification disclosure is objected to along with the claims because of inconsistencies in naming of chemical compounds or enzymes. In the specification, applicants use capital letters and small letters to name the same chemical compounds (acids, buffers, metals) or enzyme and also chemical notation along with complete names in the text. As with the difficulties in the claims, the specification refers to chemical compounds and trademarked items in various ways (DTT, dithiothreitol, etc.) and the lack of consistency presents difficulties for locating proper support for amendments, etc. Appropriate correction is required.

(b) The objection to the specification for a lack of section titles is withdrawn.

(c) The objection to the specification regarding page number is withdrawn.

(d) The last paragraph of the specification has been amended to remove the incomplete sentence, thus this objection is withdrawn.

(e) The objection to the font of the specification is withdrawn.

(f) The objection to the specification regarding proof reading is withdrawn.

(g) The specification is objected to because trademarks are disclosed throughout the instant specification. Trademarks (such as Triton X-100) should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks. The examiner notes the changes made to the name Triton X-100 throughout the specification, but notes that the generic terminology previously added with the amendment of 29 January 2007 was not re-stated. Upon allowance, this will result in a printer query since the two amendments overlap but neither comprises a final draft of paragraph [0026].

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1, with dependent claims 4-6, 8-10, 12-14, 16-20, 23-26, 33-46, 48-50, 64-65, is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear what method steps applicant intends the method to comprise, and in what order, with the current recitation in claim 1. Claim 1 recites that the method comprises "exposing the blood sample to an enzyme-detergent combination comprising plasminogen, streptokinase, phospholipase A2 and DNase, wherein the plasminogen and streptokinase is [sic] maintained in a frozen state until exposure of the blood sample to the enzyme-detergent

combination". However, it is unclear if the PLA2 and the DNase are also in the frozen mix with the plasminogen and the streptokinase.

Also, claim 1 recites that the "streptokinase reacts with plasminogen upon thawing". It is unclear if the streptokinase and plasminogen frozen mix (with the PLA2 and DNase?) is thawed, allowing them to make plasmin, and then added to the blood sample or if the mix (plasminogen, streptokinase, PLA2 and DNase) is added to the blood sample in a frozen state and then, as it thaws in the blood sample, plasmin is made.

It is unclear what is intended to be claimed with the terms "metabolic markers", "cancerous matter", and "disease state markers". These are not art accepted terms and the metes and bounds of the claim comprising them are unclear. The specification discloses that cancerous cells are encompassed, but does not appear to define or further discuss "cancerous matter", "disease state marker" and "metabolic marker". It is noted that there are multiple iterations of this list and some disclose "pathogenic and native disease state markers" and "chemical agents", which are not recited in the claim. However, there is no explanation of what applicant intends these terms to encompass in light of the enormous number of "particles" associated with "markers" or "matter".

Claim 6 is rejected because the aqueous salt solution composition is unclear. The specification discloses at [0018] that the aqueous salt solution may comprise NaCl and NaPO4, but does not disclose Na3PO4.

The rejection of claim 11 is withdrawn in view of the cancellation of the claim.

Claim 12 is rejected as depending from cancelled claim 11. For the purposes of this examination, claim 12 has been interpreted as depending from Claim 1.

Also, claim 12 recites that "the plasminogen and streptokinase are mixed and distributed" into test containers. It is not clear if the PLA2 and DNase from claim 1, which presumably are mixed with the plasminogen and streptokinase, are present in the mix and the containers or are added to the mix at a later method step.

Claim 16, with dependent claims 17-20, 23-26, 33-43, 50, is rejected because it is unclear in what sequence the resuspension, thawing and adding take place. Is the combination added to the buffer solution while frozen, with the buffer aiding in thawing, or is the combination thawed and then added to buffer and then added to the whole blood sample, or is the frozen mix added to the buffer and then the buffer/mix added to the blood sample while still frozen and the thawing allows some process among all three reagents to occur.

Claim 17 is rejected because the claim recites the limitations of an amount of endonuclease and an amount of lipase. There is insufficient antecedent basis for this limitation in the claim. Claim 17 is dependent from claim 16, which is dependent from claim 1 and there is no claim in the chain that recites the presence of endonuclease or lipase. Claim 1 now recites pLA2 and DNase, but not the others.

Claims 23-26 are rejected because it is unclear with what enzyme(s) the pellet is being "digested". Claim 16 recites that the enzyme-detergent mix is added to a buffer and the whole blood sample and is incubated, claim 23 then recites that the sample mixture is centrifuged to form a supernatant and a pellet and the supernatant is decanted with the pellet then being digested. It is unclear if the enzymes present in the mix are intended to be part of the pellet, i.e., if the centrifuging step requires sufficient time to pelletize all the elements of the mix with the enzymes already present digesting elements of the pellet or if new enzymes would be added in order to digest cellular material and release DNA for subsequent extraction. It is also unclear how the enzymatic digestion occurs if the centrifuged pellet lack sufficient buffer (now in the supernatant) for the enzymes, either initially added or later added, to be effective.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1, 4-6, 8-20, 23-50, 64, and 65 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the amendment to claim 1.

The rejection of claims 11-20, 23-26, 33-43, and 64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the cancellation of claim 11.

Claim 1, with dependent claims 4-6, 8-10, 12-14, 16-20, 23-26, 33-46, 48-50, 64-65, is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for particles encompassing DNA released from bacterial cells, viruses, and fungal cells, based on the experiments performed on Bacillus anthracis and Yersinia pestis cells, does not reasonably provide enablement for any analyte, encompassing prions, toxins, metabolic markers, cancerous matter, and disease state markers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant claims read on a detection method encompassing the discovery of any particle from a list of types of biological "matter" or "marker". Thus, the claims read on detecting almost any biological element. The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art. The instant specification is not enabling for claims drawn to particles of DNA from cells of various kinds.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by

weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In the instant case, (1) the amount of experimentation is enormous because the claims as recited encompass detecting any particle from any cancerous, methabolic, or disease state biological matter or marker as well as any prion or toxin present in any blood sample; (2) the amount of guidance provided by the specification is not large since the only two concrete examples are for DNA from B.anthracis and Y.pestis. One of skill in the art would have no idea what structural characteristics might make one type of matter or marker react in the current method, another interfere with or inactivate the assay components, or another have activity at all. Continuing, (3) the specification is lacking in working examples, indeed much of the specification appears to be general descriptions of what one of skill "may" do; As for the next Wands factor, (4) the nature of the invention is detection of particles, particularly DNA particles, however the claims are drawn to the detection of any particle related to prions, toxins, cancer, metabolism, and disease. The prior art (5) shows that prions, particularly, are hard to detect and differentiate from other proteins and there appear to be no particular steps to perform these differentiations. Also known is that toxins may comprise many types of biological, chemical, or physical entities and how this method could be applied to any type of toxin, a radioactive compound, for example, is not made clear. (6) The relative level of skill in this art is very high;

(7) the predictability of the art is low given that detection of any disease element, particularly any cancerous matter, is known by those of skill in the art to be problematic. Finally, (8) the claims are enormously broad.

Based on this analysis, the conclusion that it would require undue experimentation to practice the instant invention is inescapable.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 10, 12, 16, 18, 19, 33, 44-46, 50, 64, and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson (J. Clin. Microbiol, 1978) in view of Dupe et al. (Thrombosis and Haemostasis, 1981).

Watson et al. teach a method of trapping bacteria from blood sample in a clot, then digesting the clot buy adding streptokinase, and culturing the bacteria for identification; where they add this blood to a medium containing sodium taurocholate which is a bile surfactant, reading on a detergent, and which also contains 100 U streptokinase (see page 123, column 2, to page 124, column 1). The method used in Watson is congruent with the procedure described in the specification (see [0045] and [0046]). Regarding the limitation that the sample is exposed to plasminogen, the whole blood sample must be inherently exposed to plasminogen because blood is known to contain plasminogen, and streptokinase would not dissolve clots without activating

downstream plasminogen. Watson particularly comments that "[i]solation from blood clot is far more reliable, provided rapid lysis occurs, since organisms trapped within the clot are susceptible to serum factors adsorbed to the fibrin meshwork" (p. 126, col. 1).

Watson et al. do not expressly teach maintaining plasminogen and streptokinase in a frozen state, or that the solution comprise NaCl, or that the streptokinase/plasminogen should be kept in a dried state, or that the plasminogen and streptokinase are resuspended in a buffer solution and added to blood and incubated at room temperature, or that the mixture should be centrifuged, the supernatant decanted, and the pellet washed.

Dupe et al. teach a method of assaying thrombus dissolution by streptokinase/plasminogen complexes in whole blood; where the streptokinase and plasminogen can be prepared ahead of time; where plasminogen and streptokinase were both available in a pharmaceutical grade lyophilized powder (see pages 530-531). The companies that provide the composition mixed them and ship them in containers (see page 530). Regarding the limitations recited in claims 18 and 19, practice of separating clots from serum by centrifugation has been well established in the art of clinical hematology.

Claims 50, 64 and 65 are included in this rejection because the enzyme-detergent combination can comprises an enzyme that can break down a nuclear membrane (claim 64) and the method can be conducted at pH 7.8 that is close to the normal pH of blood that is pH of 7.4 (claim 65).

A person of ordinary skill in the art at the time the invention was made would have been motivated to prepare streptokinase and plasminogen in either a frozen or lyophilized form because Dupe et al. teach that they can be stored for longer periods of time preserved in such

manner, and Watson et al. teach that streptokinase is useful reagent for isolating bacteria from blood cultures and that various serum factors may be needed to work with the streptokinase.

Hence, it would have been prima facie obvious tone of ordinary skill in the art at the time the invention was made to freeze or lyophilize streptokinase and plasminogen to store for later use in a method of isolating bacteria.

Claims 1, 10-12, and 44-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson (J Clin Microbiol, 1978) in view of Smith et al (Thrombosis and Haemostasis, 1982).

The teachings of Watson are discussed above and applied as before.

Watson et al do not expressly teach that enzymes are freeze dried for storage.

Smith et al teach that plasminogen and streptokinase can be separately purified and lyophilized in individual containers for long-term storage (see "Fibrinolytic agents", p. 269, col. 2, for example).

A person of ordinary skill in the art at the time the invention was made would have been motivated to lyophilize plasminogen and streptokinase because Smith et al teach that these enzymes retain activity when preserved in this manner, and preservation allows for long-term storage of useful reagents.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to lyophilize streptokinase and plasminogen in preparation for isolating bacteria from blood in the method of Watson.

Claims 1, 10, and 44-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson (J Clin Microbiol, 1978) in view of Cassels et al (Biochem. J., 1987).

The teachings of Watson are discussed above and applied as before.

Watson does not expressly teach the use of phosphate in a storage solution.

Cassels et al teach that phosphate is a suitable medium for carrying out reactions comprising plasminogen and streptokinase (see "Clot-lysis assay", p. 396, col. 2, for example). They also teach a method of adding plasminogen/streptokinase combination into an assay medium containing Tween 80, a detergent. They test the efficacy of the enzyme combination by measuring the radioactive iodine remaining in the plasma, a type of blood sample. This is a measure of how much fibrin was cleaved by the streptokinase/fibrinogen (see Material and Methods, p. 396, col. 2, for example; by measuring radioactive iodine-containing particles released, i.e., separating cleaved from noncleaved fibrin, Cassels et al.. could measure enzymatic activity. Additionally, it is standard practice in the art of protein purification to snap-freeze proteins in phosphate-buffered saline, for example, for storage. A person of ordinary skill in the art at the time the invention was made would have been motivated to freeze streptokinase in a phosphate buffer because Cassels et al teach that a phosphate buffer is compatible with streptokinase activity, and it is well-known in the art to freeze proteins in a phosphate buffer such as PBS, for example.

Hence, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to freeze streptokinase in a phosphate buffer.

Claims 1, 10, 12-14, 16, 18, 19, 44-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson et al. in view of Dupe et al. and further in view of Kreilgaard et al. (1998).

The teachings of Watson and Dupe are disclosed above where they do not expressly teach the lyophilization of streptokinase or plasminogen in trehalose.

Kreilgaard et al. teach that trehalose can be added to a protein before freeze drying process and that trehalose affords protection to enzymes during freeze drying and storage as dried solid (see page 121, column 2, fro example).

It would have been obvious to one of ordinary skilled in eth art at eth time the invention was made to include trehalose in a method of freeze drying an enzymatic combination taught by Dupe et al. because Dupe et al. teach that it is possible to freeze dry enzyme in separate vials and Kreilgaad et al. teach that trehalose is useful sugar to add to an enzyme composition before freeze-drying. One would be motivated to do so for the expected benefit of protection of particles.

Claims 1, 8, 10, 16, 18, 19, 23-26, 33, 34, 44-46, 49 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson (1978) in view of Zhang et al (J. Clin. Microbiol., 1995) in view of Dupe et al (1981), in view of Zierdt et al (1977) and in view of Hallick et al (Nucleic Acid Res, 1977).

The teachings of Watson (1978) and Dupe et al (1981) are discussed above and applied as before.

Zhang et al. teach a method of collecting blood from patients. The blood is then broken up with buffer ATL which comprises SDS and proteinase K. The purified DNA is then subjected to PCR amplification, successfully showing the presence of Streptococcus pneumoniae DNA in patients' blood (see Materials and Methods, p. 597, see Results, p. 599, and see Table 3, p. 600, as examples).

Additionally, Zhang et al teach that blood samples can be lysed using glass beads and vortexing, and then centrifuged to remove gross blood byproducts before the supernatant is decanted and processing continued with a Qiagen blood mini amp kit (see Materials and Methods, p. 597, for example). The Qiagen blood mini amp kit teaches the use of proteinase K and SDS as components of the process of purifying DNA from blood samples (see Qiagen DNA blood mini kit handbook, p. 12, for example). Also as discussed above, Zhang et al teach the use of citrate as an anticoagulant.

None of the above references expressly teaches the use of endonuclease inactivation, DNAse inactivation, or addition of aurintricarboxylic acid to the sample.

None of the references teaches the inclusion of octylphenol ethoxylate (Triton X-100).

Hallick et al teach that aurintricarboxylic acid (ATA) is a general nuclease inhibitor (see Introduction, p. 3055, for example). They demonstrate that addition of ATA to a nuclease reaction inhibits the reaction (see Figs 1 and 2, p. 3058, for example). Additionally they suggest that it would be useful to add ATA to prevent degradation of nucleic acids during nucleic acid isolation (see Introduction, p. 3055, for example).

Zierdt et al (1977) teach that Triton X-100 is advantageously added to a blood solution in a method of purifying bacteria present in the blood. The procedure allows one to lyse blood cells without damaging the bacteria (see Materials and Methods, p. 46, col. 2, for example).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add ATA and Triton X-100 when performing the assay of liberating particles, because Zhang et al teach that one can perform PCR from purified bacterial DNA, Zierdt et al teach that one can isolate bacteria from whole blood in a method comprising Triton X-100, and Hallick et al teach that addition of ATA inhibits nucleases and suggest its usefulness when one desires to purify DNA. One would have been motivated to do so for the expected benefit that using ATA and Triton X-100 would provide higher yields of quality DNA.

Based upon the teachings of the cited references, the level of skill of one of ordinary skill in the art, and absent any evidence to the contrary, one would have a reasonable expectation of success in practicing the claimed invention.

Claims 1, 8, 10, 16, 18, 19, 23-26, 33, 34, 39, 44-46, 49, 50, 64, and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson (1978) in view of Zhang et al (1995) in view of Dupe et al (1981) in view of Hallick et al (Nucleic Acid Res, 1977) and in view of Zierdt (J Clin Microbiol, 1982).

The teachings of Watson (1978), Zhang et al (1995), Dupe et al (1981), and Hallick et al (1977) are discussed above and applied as before.

None of the references expressly teaches the use of 10 mM potassium phosphate.

Zierdt teaches that the buffer should contain 10 mM sodium phosphate (see p. 172, col. 2, for example).

A person of ordinary skill in the art at the time the invention was made would have been motivated to use potassium phosphate in a method of isolating bacteria because Zierdt teaches that a 10 mM sodium phosphate buffer is suitable in a method of isolating bacteria from blood, and potassium phosphate is a suitable equivalent.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use a 10 mM potassium phosphate buffer in a method of isolating bacteria from blood.

Applicants Responses

Applicant asserts that the Watson reference does not teach a method of trapping bacteria from a blood sample in a clot, digesting the clot by adding streptokinase, and culturing bacteria for identification wherein the medium comprises sodium taurochlorate (a bile surfactant). Applicant argues that the inclusion of specific names of particles that could be detected by the instant method distinguish the claims over the prior art. Applicant's arguments filed 21 July 2008 have been fully considered but they are not persuasive. The Watson reference clearly teaches the identification of bacterial particles from whole blood in a method comprising the use of streptokinase, serum factors that are part of the fibrin matrix, and sodium taurochlorate, therefore rendering obvious the base method of the claims, with the additional references teaching methods comprising the various specific steps.

Conclusion

Claims 4-6, 17, 26, 36-38, and 48 are free from the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa J. Hobbs whose telephone number is 571-272-3373. The examiner can normally be reached on Hotelling - Generally, 9-6 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lisa J. Hobbs/
Primary Examiner
Art Unit 1657

ljh